present knowledge of their relative histologic structure. I remember Theodor Kocher (when I was with him) attached the greatest importance to the study of the histogenesis of toxic goiter in arriving at a proper classification. But the biochemistry of this disease has yet to be satisfactorily worked out, and our present knowledge of it leaves much to be desired. The very fact that a hypertoxic thyroid may contain adenomata and that an adenomatous thyroid may contain areas of so-called hyperplastic structure, which may greatly modify the symptoms, lends confusion to any categorical effort in classification. Until we have a better histologic or chemical basis for definite differentiation in these two major clinical forms of toxic goiter, the ones given by the author and generally accepted must suffice.

From what we do know it is obvious that one who would successfully treat this disease of the thyroid gland must have given years of thoughtful study to the subject and have acquired a seasoned judgment based on a large clinical experience with toxic goiters. One can only wonder at the casual manner in which the empiricist will reach for Lugol's solution, or advise and undertake operation with little or no preliminary study or preparation of the patient for operation. Irreparable damage may be done to a patient who might otherwise have been a favorable subject for surgery, by the prolonged and unintelligent use of iodin. Such a patient cannot be reëstablished by the resumption of iodin preparation, and a patient who might have been a favorable risk, if iodin had not been given at all or if only given for the usual preparatory period, has been changed into a very hazardous risk by excessive iodinization. The author has placed a very proper emphasis upon this abuse of iodin.

The hot, smooth, soft, pulsating tumor; the thrill, the digital tremor and moist palms, the nervous, restless, anxious attitude—it is not necessary to have exophthalmos to properly classify the form of goiter from which this young patient is suffering. The nodular tumor of slow development without remissions, but with high blood pressure and metabolic rate under 50 with toxic symptoms coming on late, may easily be named an adenomatous goiter. Between these extremes of definite symptomatology are the cases in which a modifying histology as well as symptomatology will form a more or less confusing picture.

Every case of toxic goiter must be individually studied. The class in which its anatomical structure, predominating symptoms and laboratory tests place it will determine for the experienced surgeon the method of treatment which will offer the patient the safest and surest relief.

X-RAY THERAPY IN DERMATOLOGY *

By LOUIS F. X. WILHELM, M. D.
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DISCUSSION *by H. J. Ullmann, M. D., Santa Barbara; Douglass W. Montgomery, M. D., San Francisco; Irving R. Bancroft, M. D., Los Angeles.*

THE epoch-making discovery of x-rays by Conrad Roentgen [1] in 1894 and the publication of his work in 1895 was followed by a period devoted to a study of their practical application in medicine. Soon it was found that x-rays were of value in the treatment of skin diseases. Various parts of the world reported new indications for their use. Freund and Schiff [2] in Vienna, Walsh,[3] Morris [4] and Sequeira [5] in England, Oudin, Barthelmy and Darier [6] in France, and Pusey [7] and Williams [8] in this country were pioneers in this promising new field of therapy. For a number of years the use of x-ray therapy was increased so as to include almost every type of dermatologic condition. In fact roentgenologists were ready to apply x-ray treatment to every skin lesion without even attempting a diagnosis. Then quite suddenly the x-ray almost was thrown into discard on account of many disagreeable complications due to the want of measured dosage. The introduction of the Coolidge vacuum tube and the perfection of a reliable ammeter and voltmeter soon followed. These instruments combined with Wehnelt and Benoist's penetrometer, Sabouraud-Noire pastilles. Holzknecht and Corbet's radiometers allowed direct measurement of current. MacKee and Remer,[9] using these aids to standardization, evolved the method of indirect dosage now in general use. The MacKee [10] skin unit is the amount of x-ray necessary to cause a temporary epilation of the scalp hair. It is four-fifths of the minimum erythema dose.

PATHOLOGY

The pathology of x-ray therapy of the skin was studied by Highman and Rulison [11] of New York. The elastic tissue, the glands, and the normal proliferative power of the skin are affected. The arterioles lose their elasticity and the corium tends to atrophy. The effect of x-ray therapy on the skin parallels from beginning to end the picture of scleroderma and, if more marked, the picture of xeroderma pigmentosum. These pathologic changes are slowly progressive and usually require years to develop to the fullest degree. Epithelioma is in a large percentage of instances the ultimate change.

The impression has obtained for many years that blonds are more susceptible to x-ray therapy than brunettes. The appearance of marked pigmentation following one-fourth skin unit (MacKee) of x-ray in several brunettes prompted the interesting paper of MacKee and Eller [12] on the variation of skin tolerance. One of these patients, a brunette about twenty-five years old, was treated at the Vanderbilt Clinic, New York. Following this reaction we treated three areas of skin one centimeter square on her forearm with one-fourth, one-half and three-fourths skin units x-ray and found pigmentation in each area. Subsequently toleration tests were carried out in 210 patients and over 40 per cent showed some pigmentation following one-fourth skin unit (MacKee) x-ray. MacKee and Eller conclude that there is a considerable variation of susceptibility to x-rays caused by age, location, complexion and inaccurracies of the best technique. Patients should be inspected carefully during a course of x-ray treatments for premonitory signs of reaction, for even a mild reaction may be followed occasionally by undesirable late effects.

INDICATIONS AND LIMITATIONS

The experience gained from years of study of the effects of x-ray treatment has taught us some limitations as well as contraindications to its use. While originally the x-ray alone was employed in the treatment of many skin diseases, today we look upon x-ray as only a part of our treatment

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plan. Local and internal measures that are indicated are employed in conjunction with x-ray therapy. Care must be exercised not to use irritating topographic applications such as tincture of iodin and ammoniated mercury before, during or immediately following a course of x-ray treatments, because this usually causes an intensification of the x-ray effect.

X-ray is most useful in subacute and chronic conditions of the skin associated with cellular proliferation. Its action is also of definite benefit in certain types of bacterial and fungus infection of the skin and its appendages. It is definitely contraindicated in conditions associated with atrophy.

DISEASES IN WHICH X-RAY IS INDICATED AND CONTRAINDICATED

Acne vulgaris, especially the deep nodular type, lends itself well to treatment with the x-ray. Originally Witherbee and Remer [13] recommended the use of twelve to sixteen weekly exposures of one-fourth skin unit (MacKee) x-ray. Experiences, as the following case citation, have modified this view.

In New York I saw an actress, age twenty-four years, brunette, who two years previously had had twelve treatments of one-fourth skin unit (MacKee) x-ray at weekly intervals. She returned on account of a recurrence of the acne. We were more interested in the patches of telangiectasia and associated atrophy found on both cheeks.

As a consequence today we give a maximum of six to eight weekly exposures of one-fourth skin unit (MacKee) x-ray or a total of one and one-half to two skin units. If this amount of treatment fails to clear up the acne we resort to the ultra-violet ray in conjunction with topographic applications and measures directed to the general condition of the patient rather than risk producing permanent skin changes.

Superficial pyogenic infections as paronychia, furuncle, carbuncle, cellulitis, phlegmon, and erysipelas lend themselves well to x-ray treatment. It is better to use one-half to one skin unit (MacKee) x-ray in these conditions. The effect is prompt, it lessens pain, diminishes local edema, and shortens the course of infection. Fitting local and general measures should be used in conjunction with the x-ray.

Fungus infections of the skin respond to x-ray treatment after they have passed through the acute and subacute stages into the eczematoid ringworm stage of Fordyce. Ringworm of the scalp and nails is also most favorably influenced by the x-ray.

Recently I saw a patient who had had a great number of x-ray treatments for ringworm of the nails. The fingers of both hands presented a marked radiodermatitis consisting of telangiectasia, atrophy and preëpitheliomatous ulceration. Evidently the threshold of tolerance had been greatly exceeded causing this unhappy complication. The social life of this patient, who is a doctor's wife, has been literally ruined. Scrupulous attention to detail and limitation of the use of x-ray within the bounds of skin toleration will eliminate this dreadful complication. Over four thousand successful epilations for tinea capitis have been done at the Vanderbilt Clinic, New York, without the production of a single permanent alopecia. Suitable topical applications should be used in conjunction with the x-ray in treating the various fungus infections of the skin.

One of the most intractable conditions in dermatology, *psoriasis,* has certain phases in its manifestation which respond well to x-ray treatment. In fact all phases of this disease react favorably to the x-ray. Due to the tendency of this disease to recur, however, x-ray is not the method of choice in the treatment of psoriasis. When the x-ray has proved itself successful in clearing up an attack of psoriasis it is hard to persuade the patient to return to the use of topographic application of ointments in future attacks. In Doctor Fordyce's office in New York I saw a patient who had had from one to two x-ray treatments every week for one and one-half years. The patient was a man forty-five years of age, strong and sturdy, a plumber by occupation. When dressed he looked perfectly normal. But when stripped of his clothes there was an entirely different picture. Telangiectasia, sclerodermatous thickening and atrophy of the skin, and several chronic ulcerations with definite epitheliomatous change were found on his trunk, arms and legs. Apparently, with his mind intent on clearing up the psoriasis, this roentgenologist did not consider the fact that the skin has definite limits of toleration to x-ray therapy. Recently I saw a young girl twenty-two years of age who had had six months' treatment with x-ray for a psoriasis of the arms and legs. Her arms and legs now show an extensive telangiectasis with beginning atrophy in addition to several scaling patches of active psoriasis. For every recurrence of psoriasis a greater amount of x-ray is necessary to cause involution of the lesions. Therefore the risk of producing undesirable skin changes is too great to use x-ray routinely in the treatment of psoriasis. X-ray and radium can be used, however, in treating localized patches of the disease. Fractional doses of x-ray are also of benefit in treating psoriasis of the nails.

Pigmented nevus and *vascular nevus* usually respond to a massive well-screened dose of x-ray. *Keloid* within the first year of its appearance will do well on filtered x-ray treatment. Care must be exercised not to overstep the bounds of toleration. A patient I saw in New York who had had a linear keloid involving the arm and the proximal part of the forearm treated with x-ray, developed telangiectasia, sclerodermatous thickening and two small ulcers. The borders of the latter manifested definite epitheliomatous change. In our enthusiasm to remove an unsightly keloid we must not use x-ray beyond the point of skin tolerance.

Mycosis fungoides is one condition in which x-ray must be pushed to the point of producing definite skin changes in order to be of real therapeutic value. The late Doctor Fordyce has shown that combining intravenous arsphenamin with x-ray treatment greatly enhances the action of the latter. He had one patient under observation for ten years without signs of recurrence after hav-

ing used this combined treatment. This is one generalized chronic disease of the skin in which we use x-ray beyond the usual point of skin toleration.

Eczema, especially the chronic lichenified type, and neurodermitis respond promptly in the vast majority of cases to fractional x-ray treatment. If the underlying cause of the condition is determined and removed the result obtained is permanent. Usually not more than six treatments of one-fourth skin unit (MacKee) x-ray are necessary to produce the desired effect. Additional x-ray treatment may be used with careful attention to detail.

Acne keloid, multiple warts respond well to x-ray treatment. In these conditions filtered x-ray is preferred. Fewer and larger doses are indicated.

Lupus vulgaris and *lupus erythematosus* do not respond well to x-ray therapy. Recently MacLeod[14] condemned its use in lupus vulgaris because it is impossible to destroy lupus tissue without causing an x-ray burn followed possibly by epithelioma. Stokes[15] reported a case of lupus vulgaris we observed at the Mayo Clinic in which hundreds of doses of x-ray had been given. The cartilages and bone of the alae nasi and the septum were lost in a dry and odorless mass of cauliflower-like vegetations of epithelioma. He advises emphatically against the use of x-ray in lupus vulgaris. Lupus erythematosus produces atrophy, therefore x-ray is contraindicated.

Keratosis senilis and the various types of *epithelioma* of the skin respond favorably to massive doses of x-ray. One or two exposures of two to four skin units (MacKee) x-ray are usually required to produce complete involution of the malignant process. The surrounding skin must be well screened to within one-half centimeter of the borders of the lesion. About ten years ago at the Vanderbilt Clinic, New York, a patient was given three skin units (MacKee) x-ray on a superficial epithelioma of the face. As far as could be determined clinically, complete involution followed. Five years later, however, the patient returned with a little fullness at the site of the former malignancy and a biopsy was taken. Doctor Satenstein showed us the microscopic section. Although the epidermis and upper cutis were free from pathologic infiltration, there was unmistakable evidence of epithelioma in the lower cutis. The only logical explanation is that some of the malignant cells were not destroyed by the x-ray and lay inactive in the lower cutis for five years. For this reason Doctor Fordyce recommended removal of the growth by electrodessication and the curette before application of the x-ray to the base of these lesions.

CONCLUSIONS

1. X-ray is not a panacea for all skin diseases.
2. X-ray should constitute only a part of our therapeutic armamentarium for skin diseases.
3. X-ray if properly controlled is the most useful agent we possess for the treatment of diseases of the skin.
4. A positive diagnosis, plus discovery of the underlying etiology of the condition presented, if possible should precede x-ray therapy in all dermatologic conditions.
5. Skin toleration tests to discover individual susceptibility to x-ray add a positive safeguard against undesirable reactions.
6. Patients should be inspected carefully before each x-ray treatment for premonitory signs of intolerance.
7. Dosage should be accurately controlled by scrupulous measurement of spark gap, skin distance, milliamperage, and time of exposure.
8. When using fractional dosage a total of two skin units (MacKee) x-ray should be the maximum amount of treatment used during a period of two months.
9. X-ray should not be used in treating generalized psoriasis.
10. Skin tolerance must not be regarded as a limiting criterion in treating mycosis fungoides with the x-ray.
11. Irritating topographic applications must be avoided before, during and after a course of x-ray treatment.
12. X-ray preferably should be used in conjunction with electrodesiccation and curettage in treating cutaneous malignancies.

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DISCUSSION

H. J. ULLMANN, M. D. (1520 Chapala Street, Santa Barbara).—I was much interested in this paper, especially from the standpoint of dosage. I believe that

if more accurate methods of measurement were employed by the average roentgenotherapist fewer untoward results would occur. Few roentgenologists would report voltage in terms of spark gap today. Eight years ago when I tested a number of machines in Chicago to determine if possible why there should be such a variation in time required with different machines to obtain the same results, I found a surprisingly large variation in voltage used, although the operators were using the same gap. Using the MacKee formula I found that if the operator of Machine D should change to Machine A and using the same gap should give the same number of milliampere minutes, he would actually give 30 per cent more than he expected. This work was reported in the April, 1921 issue of the *American Journal of Roentgenology,* and since its publication it has become common practice for roentgenologists to report their dosage in volts rather than in "inches gap." To measure voltage by "gap" is equivalent to measuring skin target distance with a rubber band.

I believe that the dosage given for epitheliomata is too low. Doctor Wilhelm spoke of a recurrence after three units. I now give from five to fifteen units or more (unfiltered), depending on the thickness of the lesion, in one or two sittings a day or two apart and consider the results excellent. There is little or no scar.

I wish to recommend this paper to everyone using x-ray, for the warnings are very timely and much needed. Overdosage in skin therapy for nonmalignant conditions is common.

I suggest that if a case of mycosis fungoides does not respond well to unfiltered x-ray that copper filtered, high voltage radiation be tried. I have one patient referred to me by Doctor Koetter, who has had marked relief from the short-wave radiation after failure of the long. This was tried following a report in the London *Lancet* of a case successfully treated by heavily filtered radium.

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Douglass W. Montgomery, M. D. (323 Geary Street, San Francisco).—Physicians are constantly employed handling, in an intimate way, highly infective viruses, in administering strong and destructive inorganic and vegetable poisons, and in applying dangerous physical tools and agencies. Accidents in the use of these drugs and agencies are bound to occur, sometimes affecting the physician and sometimes the patient. The reaction of the public to these accidents is interesting. Physicians, for example, from the nature of their occupation, are more exposed to the virus of influenza than the rest of the population, and the death incidence among them from this cause is the highest in the community. The public, however, is not moved by this. If, however, an unfortunate result occurs in the employment of x-rays, the public may assess the physician for heavy damages, even to ruining him financially, and no thought is given to the daily risks he runs in serving the public either in this or in any other of his capacities. And yet the public demands the service. The public feels so acutely outraged by these and like accidents that legislatures, for instance, have repeatedly passed stringent laws forbidding the employment of all poisons. *Demos,* however, soon finds that the expert handling of the interdicted poisons and potent physical agents is necessary in our intricate civilization, and the laws fall into desuetude. The type of mind remains, however, and the old secular growl against the profession also remains. X-rays now seem to be particularly obnoxious to the public, and in view of this it might be a salutory exercise for any physician employing them to read over Doctor Wilhelm's paper once a day in lieu of other devotions. He might also bear in mind that the patient begging for relief from an annoying or dangerous trouble is an entirely different creature from the same person suing for damages.

When tempted by the pleadings of a patient suffering from such a persistently recurrent disease as psoriasis, for example, one may remember Saint Paul's advice: "Be as wise as a serpent and as harmless as a dove."

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Irving Bancroft, M. D. (812 Detwiler Building, Los Angeles).—A roentgenologist once said in my presence: "I don't know a single thing about skin diseases. All I know is that a patient has a skin disease and I apply the x-ray and the disease gets well." Shortly after that my medical defense insurance premium was raised 150 per cent a year because I used an x-ray machine. So, measured by the yardstick of insurance premiums, we, as a class, are labeled as lacking in knowledge. This realization of a lack of knowledge has developed a group of small-dosage roentgenologists similar to the physician who treated a woman with x-ray every other day for over two years. Her trouble was pruritus ani, and at the end of the treatments she still had her rectal hair.

The skin unit or erythema dose, as a measure of x-ray quantity, is inaccurate, and yet it is more convenient than the R unit, which is based on the amount of rays emanating from a given amount of radium in a given time, or the H unit based on the change of color of a chemical substance. Originally a "foot" or a "cubit" was nearly as inexact. The skin unit should be more clearly defined in terms of R, which at the present time is the most definite measure which we have. Until that time comes we should remember that one skin unit is about equal to 1000 R or 5 H.

The object of x-ray skin therapy is to provoke a colloidal modification of the atoms of the cells and thereby to initiate a physiological change. Experiments have proved that rays of different wave lengths have different physiological effects. German and French authorities, especially Regund, Soloman, and Wetterer, advise the use of a filter of aluminum in all cases of superficial therapy. The reason for this is that a highly filtered ray causes less harmful epithelial modification, and the dermatitis that occasionally follows is very mild and heals quickly; much more so than a similar dermatitis caused by an unfiltered ray.

Several years ago attempts were made in my office to standardize two different self-rectifying x-ray machines, and after a fair trial it seemed that the voltmeter was not accurate because, as the current was alternating, only a part passed through the voltmeter, and that part was not regular and even. Physicists also say that a milliammeter is not accurate in a self-rectifying machine, as there is an inverse current which falsifies the reading. So, therefore, an interrupterless apparatus only should be used with the MacKee formulas.

In nevi of all kinds I have found other methods of destruction preferable and, although I agree that x-ray does not destroy lupus, I believe that filtered x-ray should be used, after curettage, as it favors fibrosis and lessens the infiltration of the tissue. In fact I have found this auxiliary character of x-rays one of its distinct advantages and, as Doctor Wilhelm says, "today we look upon x-ray as only a part of our treatment plan."

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Doctor Wilhelm (closing).—The discussion helped to emphasize the one point that I hoped to bring out in this paper, namely, that we use *caution* in treating the skin with the x-ray.

I wish to thank the discussers individually for their discussion.

If we succeed in preventing one case of radiodermatitis this paper will not have been in vain.